

IN THE CLAIMS:

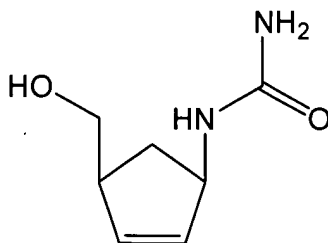
Cancel claim 23, without prejudice.

REMARKS

Reconsideration and allowance are respectfully requested. Claim 23 has been canceled without prejudice. Accordingly, claims 1-5 and 16-22 are pending and at issue.

Claims 1-5 have been rejected under 35 U.S.C. §102(b) as anticipated by Katagiri *et al.*, *Chem. Pharm. Bull.*, 39(5):1112-1122 (1991) or Taylor *et al.*, *Tetrahedron: Assymetry*, 4(6):1117-1128 (1993).

As noted in applicants' prior response, Katagiri *et al.* disclose a process for preparing 1-amino-4-(hydroxymethyl)-2-cyclopentene (compound 42) from 2-azabicyclo[2.2.1]hept-5-en-3-one (compound 1) in charts 6 and 13 on pages 1114 and 1116. As shown in Chart 6, an electron withdrawing group W is first attached to the nitrogen atom of 2-aza-bicyclo[2.2.1]hept-5-en-3-one (compound 1) to yield an *N*-substituted compound (10c). The *N*-substituted compound (10c) is reduced with sodium borohydride to yield compound 11c, which has the formula

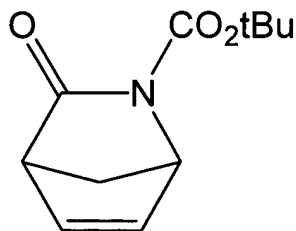


See also lines 1-4 on the right column of page 1114. Compound 11c is then reacted with sodium nitrite in an acidic medium to yield 1-amino-4-(hydroxymethyl)-2-cyclopentene (compound 42). See chart 13 and lines 15-21 on the right column of page 1116.

The Examiner notes that at page 5, lines 31-39, of the instant specification, the applicants state that an amino acid ester can be formed when the reaction is carried out in the presence of an alcohol. Applicants respectfully submit that this statement is irrelevant as to whether the presently claimed process is novel over Katagiri *et al.* Katagiri *et al.* do not disclose reacting a metal hydride with 2-azabicyclo[2.2.1]hept-5-en-3-one to form the aminoalcohol recited in pending claim 1. Rather Katagiri *et al.* react an *N*-substituted compound (10c) with sodium borohydride. Thus, Katagiri *et al.* do not anticipate the presently claimed process.

The Examiner asserts that Taylor *et al.* teach the presently claimed process at page 1123.

Taylor *et al.* teach reacting 2-azabicyclo[2.2.1]hept-5-en-3-one (compound 1b) to form an ester having the formula



See step i of scheme 3 on page 1123. The ester is subsequently reacted with sodium borohydride (NaBH_4) and $\text{CF}_3\text{CO}_2\text{H}$ to form an aminoalcohol (compound 5).

Unlike the presently claimed process, Taylor *et al.* do not disclose or suggest reacting 2-azabicyclo[2.2.1]hept-5-en-3-one with a metal hydride. Rather in Taylor *et al.*, the ester is reacted with sodium borohydride. Furthermore, Taylor *et al.* do not disclose or suggest that an aminoalcohol would be formed by reducing 2-azabicyclo[2.2.1]hept-5-en-3-one with a metal hydride.

Therefore, Taylor *et al.* do not disclose or suggest the presently claimed process.

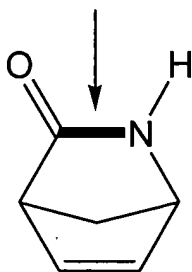
For the foregoing reasons, applicants respectfully request withdrawal of this rejection.

Claims 1-5 and 16-22 have been rejected under 35 U.S.C. §103(a) as obvious over Katagiri *et al.* or Taylor *et al.* in view of Wieczorek, U.S. Patent No. 5,847,201. Wieczorek allegedly teaches that lithium borohydride and sodium cyanoborohydride can be used as reducing agents in the preparation of aminoalcohols.

Katagiri *et al.* do not disclose or suggest that 2-azabicyclo[2.2.1]hept-5-en-3-one can be reduced with a metal hydride to yield an aminoalcohol without first converting the heptenenone into an amino acid ester. As shown by Examples 1.2, 1.3, and 1.4 of the present application, the inventors of the present invention have discovered that an amino acid ester intermediate need not be formed in order to produce an aminoalcohol from 2-azabicyclo[2.2.1]hept-5-en-3-one. In these examples, the aminoalcohol was formed by reacting 2-azabicyclo[2.2.1]hept-5-en-3-one with lithium borohydride in the absence of an alcohol. Since alcohol was not present, an amino acid ester is not formed.

In fact, Katagiri *et al.* found that it was necessary to add an electron withdrawing group W to 2-azabicyclo[2.2.1]hept-5-en-3-one in order to yield an aminoalcohol. See the last paragraph in the left column on page 1113. The aminoalcohol is formed by cleaving the amide bond in 2-azabicyclo[2.2.1]hept-5-en-3-one (see below).

The Amide Bond



Katagiri *et al.* found “that if an appropriate electron-withdrawing substituent was introduced at the amide nitrogen ... the desired reductive C-N bond cleavage reaction proceeded smoothly” (left column, lines 35-38, page 1113). Katagiri *et al.* also found that the aminoalcohol could not be formed from 2-azabicyclo[2.2.1]hept-5-en-3-one without first attaching a substituent to the nitrogen atom in the heptenenone. See lines 1-4 on the right column of page 1114 of Katagiri *et al.* and page 6, line 18, to page 7, line 6, of the April 30, 2001 Amendment.

Based on the foregoing, one of ordinary skill in the art would not have a reasonable expectation based on Katagiri *et al.* that 2-azabicyclo[2.2.1]hept-5-en-3-one could be reduced with a metal hydride to form an amino alcohol. Nor would one of ordinary skill in the art have the motivation to react 2-azabicyclo[2.2.1]hept-5-en-3-one with a metal hydride to form an aminoalcohol.

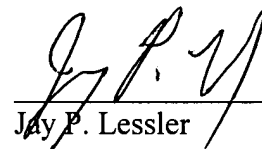
As discussed above, Taylor *et al.* do not disclose or suggest reacting a 2-azabicyclo[2.2.1]hept-5-en-3-one with a metal hydride.

Wieczorek does not discuss heptenenone compounds, such as 2-azabicyclo[2.2.1]hept-5-en-3-one. Therefore, Wieczorek does not provide any motivation or a reasonable expectation of success for reacting 2-azabicyclo[2.2.1]hept-5-en-3-one with a metal hydride.

For the foregoing reasons, Katagiri *et al.* and Taylor *et al.* alone or in combination with Wieczorek fail to render obvious the presently claimed process. Accordingly, applicants respectfully request withdrawal of this rejection.

It is believed, for the foregoing reasons, that the claims warrant allowance, and such action is earnestly solicited.

Respectfully submitted,



Jay P. Lessler

Reg. No. 41,151

Attorney for Applicants

DARBY & DARBY, P.C.
805 Third Avenue
New York, N.Y. 10022
Phone (212) 527-7700